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EXAMINER
HOWARD, ZACHARY C

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/594,920	NAKAO ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *1-19,32-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-31* is/are rejected.

7)☒ Claim(s) *20-22,26 and 29* is/are objected to.

8)☒ Claim(s) *1-51* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/06; 1/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

Claims 1-51 are pending in the instant application.

Election/Restrictions

Applicants' election with traverse of Group II, claims 20-31, in the reply filed on 3/10/08 is acknowledged.

The traversal is on the ground(s) that MPEP § 1893.03(d) states that following an election in view of lack of unity, "when all of the claims drawn to the elected invention are allowable, the nonelected invention(s) should be considered for rejoinder". Applicants quote several sentences from MPEP 1893.03 (d) regarding particular categories that should be rejoined.

This is not found persuasive because no claims drawn to the elected invention are allowable for the reasons set forth below. Furthermore, it is noted that the elected group is directed to a process and not to a product, and therefore the only category mentioned in MPEP 1893.03(d) to which an allowable claim in the elected group would be subject is "any nonelected process claim that requires all the limitations of an allowable process claim, should be rejoined".

Applicants further argue that MPEP § 803 states that "if the search and examination of an entire application can be made without a serious burden, the Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions". Applicants argue that the Examiner should rejoin at least Groups II and V "since they are closely related in subject matter".

This is not found persuasive because the "serious burden" standard is not applicable to national stage applications filed under 35 U.S.C. 371; instead these applications are subject to the unity of invention standard. In the instant case, the technical feature linking groups I-V does not constitute a special technical feature as defined by PCT rule 13.2, as it does not define a contribution over the prior art (see pg 3 of the 2/8/08 Office Action).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-19 and 32-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/10/08.

Applicant's election of the species of (1) CNP-22, (2) osteoarthritis that is degenerative gonarthritis, and (3) indomethacin in the reply filed on 3/10/08 is acknowledged.

Claims 15, 18 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 20-31 are under consideration, in so far as they are drawn to the elected species.

Specification

The disclosure is objected to because of the following informalities:

(1) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "ANTIBODY THAT BINDS A PRO1575 POLYPEPTIDE".

(2) An updated priority statement of the instant application's parent provisional and nonprovisional applications should be included in the first sentence of the specification or application data sheet. Specifically, the first sentence of the specification should be amended to indicate that the instant application is a 371 of PCT/US05/06831, filed 3/31/2005.

Appropriate correction is required.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 602. Specifically, the declaration filed on 9/29/06, at pg 1 is missing a check mark in the box "was filed as PCT international application".

Claim Objections

Claims 20, 21, 22 and 29 are objected to because of the following informalities:

(1) Claim 20 is objected to for using the abbreviation "GC-B" without the corresponding name of the referenced compound (guanyl cyclase B). When an abbreviation is used for the first time in the claims it should be spelled out completely (e.g., "guanyl cyclase B (GC-B)").

(2) Claim 21 is objected to for using the abbreviation "CNP" without the corresponding name of the referenced compound (C-type natriuretic peptide).

(3) Claims 22 and 29 are objected to because it is unclear whether "from mammals, including human" indicate that the CNP is from a single mammal (selected from a group of mammals including humans) or is from multiple mammals simultaneously (i.e., a mixture of CNP from mammals, including human).

(4) Claim 26 is objected to because the word "chondrocyte" should be plural (i.e., chondrocytes), because the method will stimulate growth of multiple chondrocytes.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20-24 and 26-30 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 20-24 and 26-30 are directed to methods that recite no particular method steps that require the hand of man. Thus, the claims encompass subject matter that includes naturally occurring *in vivo* activation of guanylyl cyclase B (GC-B) by its natural

ligand C-type natriuretic peptide (CNP). In the absence of the hand of man, a naturally occurring process is considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are directed to methods but not actually recite any positive method steps (e.g., a step of administration). Instead they merely recite an intended goal (e.g., inhibiting arthritis or promoting growth of articular chondrocytes) and a mechanism (e.g., activation of GC-B by CNP), without reciting any steps to be performed that achieve the recited goal.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-24 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting arthritis, wherein the arthritis is inhibited by activating guanyl cyclase B (GC-B), comprising administration of a mammalian or avian C-type natriuretic peptide (CNP), or a derivative that has a deletion, substitution, or addition of between 1 to 10 amino acids in the amino acid sequence of SEQ ID NO: 1 or 2 and wherein said derivative possesses the ability to bind to G-CB and increase intracellular production of cGMP, does not reasonably

provide enablement for method of inhibiting arthritis, wherein the arthritis is inhibited by activating GC-B. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention of claims 20-24 is a method of inhibiting arthritis by activating guanyl cyclase B (GC-B; also known as guanylyl or guanylate cyclase B in the prior art). The nature of the invention of claims 26-30 is a method for promoting the growth of articular chondrocytes by activating GC-B. GC-B is "also known as the type B natriuretic peptide receptor (NPR-B)" and "transduces an extracellular signal to intracellular production of cGMP" and "is the receptor for C-type natriuretic peptide" (see pg 1024 of Schulz, 2005. Peptides. 26: 1024-1034). Thus, C-type natriuretic peptide (CNP) is a specific natural ligand for the GC-B receptor.

The scope of claims 20 and 26 is such that any means of activation of GC-B is encompassed by the claims. While the specification teaches that a GC-B activator can be "peptide or a nonpeptidic low-molecular-weight compound, preferably a CNP peptide or a derivative thereof, that can bind to and activate GC-B, which is known as a CNP receptor" (pg 16), claims 20 and 26 encompass any peptide, protein, nucleic acid, lipid, carbohydrate, antibody, or other organic or non-organic compound that can activate GC-B. Claims 21-24 and 27-30 are limited to activation of GC-B by a C-type natriuretic peptide (CNP) or a derivative thereof. The specification and claims 24 and 30 indicate that a "derivative” thereof encompasses mutations that include deletions, substitution or addition of one or more amino acids to human CNP-22 (SEQ ID NO:1) or CNP-53 (SEQ ID NO: 2) and that possess a CNP activity. No limit is placed on the number of changes

as long as a "CNP activity" is present. The specification teaches that "CNP activity" includes "the activity to act on GC-B to increase guanyl cyclase activity, the activity to eliminate, inhibit or relieve arthritis including osteoarthritis, and the activity to promote the growth of the articular cartilage" (pg 19). Claims 22, 23, 28 and 29 are also considered to encompass "a derivative" of a CNP of the same scope because they depend from claim 21 or 27, and thus the recitation limits both the CNP and the "derivative"; i.e., claim 23 is broadly interpreted to encompass a CNP of SEQ ID NO: 1 or a derivative thereof.

The specification includes the following Examples in support of the claimed invention. Examples 1-5 describe construction and characterization of a transgenic mouse that overexpresses murine CNP-22. The specification teaches that these mice demonstrated "statistically significantly thicker articular cartilage (Figure 4)" and a "statistically significantly larger" "number of articular chondrocytes per microscopic field" (pg 35). Example 6 reports that the transgenic mice are more resistant to collagenase-induced osteoarthritis of the knee joint than a wild-type mouse. Examples 7 and 8 describe two experiments testing the therapeutic effect of CNP-22 infusion on osteoarthritic models. Example 7 reports that CNP-administered wild-type mice had reduced collagenase-induced knee-joint "synovial cell growth, granulation and inflammatory cell infiltration in the synovial cell membrane" as compared to a control (solvent alone). Example 8 reports that "CNPs are also effective in inhibiting arthritis in osteoarthritis caused by physical overload on the knee joint resulting from surgical procedures" (pg 38). Example 9 describes the "combined effect of nonsteroidal anti-inflammatory drug (NSAID) and CNP in collagenase OA model". Example 10 describes the effect of CNPs on adjuvant arthritis rat model and reports that CNP administered rats had a lower arthritis score and higher weight as compared to the control group. Example 11 describes the effect of CNP on collagen arthritis rat model and reports that the CNP-administered rats had less weight loss than the control group.

The specification teaches two naturally-occurring human forms of C-type natriuretic peptide (CNP), which CNP-22 (SEQ ID NO: 1) and CNP-53 (SEQ ID NO: 2). CNP-53 fully comprises CNP-22 as CNP-22 is identical to residues 32-53 of CNP-53.

The specification teaches that pig and rat CNP share the same CNP-22 sequence as humans, but have two differences (at positions 17 and 28) in the CNP-53 sequence. Chicken CNP-22 has one difference at position 9 from the pig, rat and human sequence.

The specification further teaches that derivatives of CNP-22 are described in "Japanese Patent Publication (Kokai) No. 6-9688 (1994)" and "International Publication No. WO/02/074234". These publications do not appear listed on either the 2/29/06 or 1/16/07 IDS. The Examiner has not been able locate a JPO document with the number 6-9688. Applicants are requested to submit this document if it provides support that goes beyond that disclosed in the WO/02/074234. The Examiner has located WO/02/074234 (Golembo et al) and listed it on the PTO-892 accompanying this office action. In Example 6 (pg 21-24), the '234 publication describes "CNP analogs", including truncated versions (17-mers, 15-mers, 14-mers, 13-mers, 12-mers and 11-mers) with or without 1-3 substitutions, as well as the "% relative binding" of each (Tables 2 and 3). Example 6 states that "All peptide variants were analyzed for activity using the Biotrak enzyme immunoassay … that measures the amount of secondary messenger, cyclic GMP, elicited after activation of the natriuretic peptide receptor by the peptide on C3H10T1/2 cells" (pg 22). It appears that the "% relative binding" listed in the Tables reflects the result of this assay. As shown in Table 2, even truncated variants as small as 11 amino acids in length (11-mers) retained a small degree of activity (~3-4%). However, Table 3 also shows that particular single amino acid substitutions in a 17-mer result in a relative binding that is less than zero (negative), presumably because they had less activity than the control.

In view of the teachings of the prior art (i.e., the '234 publication), the skilled artisan could practice the claimed methods with a CNP of SEQ ID NO: 1 or 2, a mammalian or avian C-type natriuretic peptide (CNP), or a derivative that has a deletion, substitution, or addition of between 1 to 10 amino acids in the amino acid sequence of SEQ ID NO: 1 or 2 wherein said derivative possesses the ability to bind to G-CB and increase intracellular production of cGMP. However, the skilled artisan would not know what additional mutations to make in the CNP and still retain activity. The

skilled artisan could make and test further mutations in a screening assay, but this would require undue experimentation in view of (1) the essentially limitless number of mutations encompassed by the claims and (2) the evidence provided by Table 3 of '234 publication that many mutations, even single substitutions, in the CNP sequence result in a loss of activity. Furthermore, the specification provides no guidance on selection of other compounds for activation of G-CB. While the skilled artisan could engage in experimentation to screen compounds in a screening assay, this too would require undue experimentation in view of (1) the essentially limitless, structurally diverse compounds that could be screened; (2) the fact that even if many compounds were screened, there is no assurance that any compounds will be found and (3) the further requirement to test each compound to determine whether there is a correlation between the *in vitro* and *in vivo* activity (as was done with CNP-22 in the instant examples).

Due to the large quantity of experimentation necessary to use the full scope of the claimed methods, the lack of direction/guidance presented in the specification regarding same, lack of working examples and the teachings of the prior art and the complex nature of the invention, undue experimentation would be required of the skilled artisan to use the claimed invention.

Claims 25 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In addition to lacking enablement for the reasons of parent claims 20 and 26, claims 25 and 31 lack enablement for the following reasons.

The nature of the invention of claim 25 is a method for inhibiting arthritis wherein the arthritis is inhibited by activating guanyl cyclase B (GC-B; also known as guanylyl or guanylate cyclase B in the prior art), and further wherein the GC-B is activated by a combination of a C-type natriuretic peptide (CNP) or a derivative thereof and at least one nonsteroidal anti-inflammatory drug (NSAID). The nature of the invention of claim

31 is a method promoting the growth of articular chondrocytes is inhibited by activating GC-B, and further wherein the GC-B is activated by a combination of a CNP or a derivative thereof and at least one NSAID. Thus the claims require that each of the CNP and the NSAID have the activity of activating a G-CB.

Example 9 describes the "combined effect of nonsteroidal anti-inflammatory drug (NSAID) and CNP in collagenase OA model" (pg 38-39). In this example, CNP, indomethacin (an NSAID), the combination of the two, or a control was administered to a mouse model of osteoarthritis (induced by knee injection of type II collagenase). The specification teaches that "the group given the combination of CNP and indomethacin showed significantly stronger inhibition for the swelling of knee joints compared to the group given the CNP alone (Figure 11)" (pg 39). Importantly, the specification also reports that "indomethacin when used alone was not inhibitory for the swelling of knee joints" (pg 39).

The results of Example 9 support the other results in the Examples that show treatment of arthritis and promotion of chondrocyte growth in response to administration of CNP-22. Furthermore, Example 9 supports that co-administration of indomethacin with CNP-22 produces an additional benefit over administration of CNP-22 alone. What the example does not demonstrate is that indomethacin is actually activating GC-B. GC-B is "also known as the type B natriuretic peptide receptor (NPR-B)" and "transduces an extracellular signal to intracellular production of cGMP" and "is the receptor for C-type natriuretic peptide" (see pg 1024 of Schulz, 2005. Peptides. 26: 1024-1034). Thus, CNP-22 is a specific natural ligand for the GC-B receptor. The results in Example 9 do not provide any evidence that the NSAID is actually activating GC-B. In fact, the result with indomethacin alone showing that it is not inhibitory for knee joint swelling suggests that indomethacin does not directly activate the GC-B receptor. While the results support enablement of a method of treating arthritis by co-administration CNP and a NSAID, they do not support a method that requires activation of GC-B by both CNP and the NSAID, as is currently claimed. Based on the current knowledge of the structures of the GC-B receptor, CNP-22 and NSAIDs, and in view of Applicants' results, the skilled artisan would not conclude that the NSAID can actually activate GC-B. Due to the large

quantity of experimentation necessary to determine how to use an NSAID to activate GC-B, the lack of direction/guidance presented in the specification regarding same, lack of working examples and the teachings of the prior art and the complex nature of the invention, undue experimentation would be required of the skilled artisan to use the claimed invention.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 20-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicants are claiming and what Applicants have possession of.

Claims 20 and 26 are genus claims because the claims are directed to methods of using a genus of means of activating G-CB. The genus is highly variant because a significant number of structural differences between genus members are permitted. The claims potentially encompass use of peptides, protein, nucleic acid, lipid, carbohydrate, antibody, other organic or non-organic compound, or even radiation, with the ability to activate GC-B. Claims 21-25 and 27-31 are genus claims because the claims are directed to methods of using a genus of derivatives of CNP. The claims potentially encompass derivatives with an unlimited number of mutations with respect to human CNP-22 of SEQ ID NO: 1 or CNP-53 of SEQ ID NO: 2, and with the ability to activate GC-B.

However, the specification fails to disclose any compounds with the ability to bind to G-CB and increase intracellular production of cGMP and that have a structure different than a mammalian or avian C-type natriuretic peptide (CNP), or a derivative

that has a deletion, substitution, or addition of between 1 to 10 amino acids in the amino acid sequence of SEQ ID NO: 1 or 2.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the full scope of the genus of GC-B activators or CNP derivatives. Structural features that could distinguish the GC-activators or CNP derivatives with activity beyond those CNP derivatives with 1 to 10 amino acid mutations are missing from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed” (pg 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she]

invented what is claimed" (pg 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of GC-B activators, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

While the specification discloses screening assays for identifying compounds that have the ability to ability to bind to G-CB and increase intracellular production of cGMP, such assays are not sufficient to indicate that Applicants had possession of the genus of compounds at the time of filing. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a mammalian or avian C-type natriuretic peptide (CNP), or a derivative that has a deletion, substitution, or addition of between 1 to 10 amino acids in the amino acid sequence of SEQ ID NO: 1 or 2 and wherein said derivative possesses the ability to bind to G-CB and increase intracellular production of cGMP, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (pg 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20-24 and 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakao et al, U.S. Patent Application Publication No. 2003/0068313, published April 10, 2003 (cited as reference AA on the 9/29/06 IDS).

Claim 20 recites a "method for inhibiting arthritis, wherein the arthritis is inhibited by activating GC-B". The term "inhibiting arthritis" broadly encompasses administration that inhibits arthritis from worsening, or inhibits it from occurring in the first place. Thus, the claims encompass administration to patients with or without arthritis.

Nakao teaches "[t]herapeutic agents for achondroplasia caused by cartilage growth inhibition resulting from mutations in the gene for fibroblast growth factor receptor 3 (FGFR3), comprising a substance activating guanylyl cyclase B (GC-B) as an active ingredient" (abstract). Nakao further teaches that C-type natriuretic peptide (CNP) is an example of a substance that activates GC-B and is to be administered to treat achondroplasia (¶ 9). The relevant art recognizes that 33% of patients with achondroplasia inherently experience arthritis (see pg 32 of Mahomed et al. 1998; American Journal of Medical Genetics. 78: 30-35; cited here solely to support inherency). Thus, administration of CNP to patients with achondroplasia as taught by Nakao would inherently inhibit arthritis from developing (in the 66% without arthritis) or worsening (in the 33% with arthritis) in these patients. Thus, the teachings of Nakao anticipate claim 20.

Claim 21 depends from claim 20 and limits the claim to a method "wherein the GC-B is activated by a CNP or a derivative thereof". Thus, the teachings of Nakao also anticipate claim 21.

Claim 22 depends from claim 21 and limits the CNP to "CNP-22 or CNP-53 from mammals, including human, or birds". Nakao further teaches that the CNP can be mammalian CNP-22 or CNP-53 (¶ 12). Thus, the teachings of Nakao also anticipate claim 22.

Claim 23 depends from claim 21 and limits the CNP to CNP-22 of SEQ ID NO: 1. Instant SEQ ID NO: 1 is disclosed as a human sequence; however, the specification teaches that pig and rat CNP-22 has an identical sequence (¶ 12). When referring to

CNP-22, Nakao cites a 1990 reference teaching porcine CNP-22. Therefore, the teachings of Nakao also anticipate claim 23.

Claim 24 depends from claim 21 and encompasses a derivative of SEQ ID NO: 1 with an addition of one or several amino acids. CNP-53 is a "derivative" of CNP-22 with an addition of 31 amino acids. Therefore, as Nakao teaches administration of CNP-53, the teachings of Nakao also anticipate claim 24.

Claim 26 is an independent claim reciting "[a] method of promoting the growth of articular chondrocyte, wherein said growth is promoted by activating GC-B". The instant specification demonstrates that administration of CNP-22 results in the promotion of growth of articular chondrocytes. Therefore, administration of CNP-22 to treat achondroplasia as taught by Nakao would also inherently promote growth of articular chondrocytes. Therefore, the teachings of Nakao also anticipate claim 26.

Claims 27-30 depend from claim 26 and recite the same limitations as claims 21-24. Therefore, claims 27-30 are anticipated by Nakao for the same reasons as claims 21-24.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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